What is claimed is:

1. A process for preparing trans-4-isopropylcyclohexane acid chloride comprising the steps of:
   a) combining trans-4-isopropylcyclohexane carboxylic acid with thionyl chloride in the presence of a C_1 to a C_6 organic amide to obtain trans-4-isopropylcyclohexane acid chloride substantially free of its corresponding cis isomer; and
   b) recovering the trans-4-isopropylcyclohexane acid chloride.
2. The process of claim 1, wherein the organic amide is selected from the group consisting of N,N-dimethylacetamide, N-methylpyrrolidone and N,N-dimethylformamide.
3. The process of claim 1, wherein the combining is carried out with about 1 to about 5 acid equivalents of thionyl chloride, from about 0.05% to about 10% weight of the amide to the acid, and a temperature of from about 10°C to about 60°C.
4. The process of claim 3, wherein the ratio of the cis isomer is less than about 0.03% weight to weight to the trans isomer.
5. The process of claim 1, wherein the combining results in a reaction mixture that is maintained for about 1 hour to about 5 hours.
6. The process of claim 1, wherein the combining is carried out in a solvent selected from the group consisting of aromatic and saturated hydrocarbons, esters and ethers.
7. A process for preparing nateglinide comprising the steps of:
   a) combining trans-4-isopropylcyclohexane carboxylic acid with thionyl chloride in the presence of a C_1 to a C_6 organic amide to obtain trans-4-isopropylcyclohexane acid chloride substantially free of its corresponding cis isomer; and
   b) converting the acid chloride to nateglinide; and
   c) recovering the nateglinide.
8. The process of claim 7, wherein the organic amide is selected from the group consisting of N,N-dimethylacetamide, N-methylpyrrolidone and N,N-dimethylformamide.

9. The process of claim 7, wherein the reacting is carried out with about 1 to about 5 acid equivalents of thionyl chloride, from about 0.05% to about 10% weight of the amide to the acid, and a temperature of from about 10°C to about 60°C.

10. The process of claim 9, wherein the ratio of the cis isomer is less than about 0.03% (wt/wt) compared to its corresponding trans isomer.

11. The process of claim 7, further comprising the step of crystallizing/recrystallizing the nateglinide.

12. A process for preparing nateglinide in a two phase system comprising the steps of:

a) preparing an aqueous solution of an alkaline earth or alkali metal salt of D-phenylalanine;

b) combining the aqueous solution with a water immiscible organic solvent containing trans-4-isopropylcyclohexane acid chloride, to form an aqueous and an organic phase, wherein nateglinide forms through reaction between the D-phenylalanine and the trans-4-isopropylcyclohexane acid chloride; and

c) recovering the nateglinide.

13. The process of claim 12, wherein a strong base is used to prepare the solution of the salt in water.

14. The process of claim 13, wherein the base is sodium or potassium hydroxide.

15. The process of claim 12, wherein the aqueous solution has a pH of at least about 8.

16. The process of claim 15, wherein the pH is at least about 12.

17. The process of claim 12, wherein the trans-4-isopropylcyclohexane acid chloride is substantially free of its corresponding cis isomer.

18. The process of claim 12, wherein the water immiscible organic solvent is a C_5 to a C_{12} hydrocarbon.

19. The process of claim 18, wherein the hydrocarbon is aromatic.

20. The process of claim 19, wherein the hydrocarbon is toluene.

21. The process of claim 18, wherein the hydrocarbon is saturated.

22. The process of claim 21, wherein the hydrocarbon is heptane.

23. The process of claim 12, wherein the water immiscible organic solvent is an ester.

24. The process of claim 23, wherein the ester is ethyl acetate.

25. The process of claim 12, wherein the aqueous solution contains water free of a co-solvent.

26. The process of claim 12, wherein recovering involves precipitating nateglinide, and separating the precipitate.

27. The process of claim 26, wherein the nateglinide separated is nateglinide Form Z.

28. The process of claim 12, wherein recovering involves moving the nateglinide to the organic phase, and concentrating the organic phase.

29. The process of claim 28, wherein the moving is carried out through acidification of the aqueous phase.

30. The process of claim 29, wherein the acidification results in a pH of from about 1 to about 5.

31. The process of claim 30, wherein the pH is from about 2 to about 3.

32. The process of claim 12, wherein the trans-4-isopropylcyclohexane acid chloride is prepared by chlorinating trans-4-isopropylcyclohexane carboxylic acid with thionyl chloride in the presence of a C_1 to a C_6 organic amide.

33. The process of claim 12, further comprising the step of crystallizing/recrystallizing the nateglinide.

34. A process for preparing nateglinide comprising the steps of:

a) preparing an aqueous solution of an alkaline earth or alkali metal salt of D-phenylalanine in water free of a co-solvent;

b) adding trans-4-isopropylcyclohexane acid chloride as a neat reagent to the aqueous solution to form nateglinide; and

c) recovering the nateglinide.

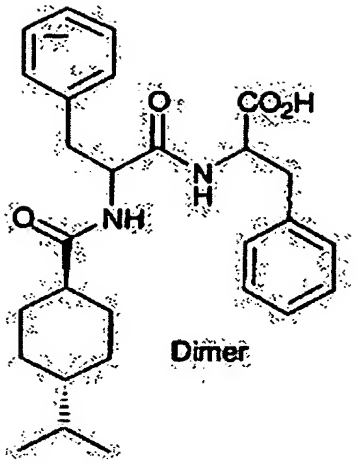
35. The process of claim 34, wherein a strong base is used to prepare the solution of the salt in water.

36. The process of claim 35, wherein the base is sodium or potassium hydroxide.

37. The process of claim 34, wherein the aqueous solution has a pH of at least about 8.

38. The process of claim 37, wherein the pH is at least about 12.

39. The process of claim 34, wherein the nateglinide recovered is substantially free of a dimer having the following structure:



Dimer

40. The process of claim 39, wherein the dimer is present at a level of from about 0.04% to about 0.1% weight of the dimer to weight of nateglinide.

41. The process of claim 34, wherein the nateglinide has a purity of at least about 99%.

42. The process of claim 34, wherein the neat reagent added contains from about 0.05% to about 8% dimethyl formamide, weight to weight of dimethyl formamide to trans-4-isopropylcyclohexane acid chloride.

43. The process of claim 34, wherein the water contains less than about 1% v/v of any other solvent.

44. The process of claim 34, wherein the trans-4-isopropylcyclohexane acid chloride is prepared by chlorinating trans-4-isopropylcyclohexane carboxylic acid with thionyl chloride in the presence of a C_1 to a C_6 organic amide.

45. The process of claim 34, wherein recovering is carried out by acidification to obtain nateglinide as a precipitate, followed by separation of the nateglinide.

46. The process of claim 45, wherein the nateglinide recovered is nateglinide Form Z.

47. The process of claim 34, wherein recovering involves moving the nateglinide to an organic phase, and concentrating the organic phase.

48. The process of claim 34, further comprising the step of crystallizing/recrystallizing the nateglinide.

49. A process for preparing nateglinide comprising the steps of:

a) combining a solution of a tri-alkyl amine salt of D-phenylalanine with trans-4-isopropylcyclohexane acid chloride in a C_1 to a C_7 amide to form nateglinide; and

b) recovering the nateglinide.

50. The process of claim 49, wherein the tri-alkyl amine is tri-ethyl amine.

51. The process of claim 49, wherein the amide is selected from the group consisting of N,N-dimethyl formamide, N.N-dimethyl acetamide and N-methyl pyrolidone.

52. The process of claim 51, wherein the amide is N,N-dimethyl formamide.

53. A process for preparing nateglinide comprising the steps of:

a) converting trans-4-isopropylcyclohexanecarboxylic acid to trans-4-isopropylcyclohexane acid chloride by reacting with thionyl chloride in the presence of an organic amide;

b) adding the isopropylcyclohexane acid chloride to toluene, heptane, ethyl acetate or mixtures thereof;

c) combining the toluene, heptane or ethyl acetate containing the isopropylcyclohexane acid chloride with an aqueous solution containing sodium salt of D-phenylalanine to form an aqueous and an organic phase, wherein nateglinide forms between the two phases; and

d) recovering the nateglinide.

54. The process of claim 53, wherein recovering involves precipitation of nateglinide followed by separation of the precipitate.

55. The process of claim 53, further comprising the step of crystallizing/recrystallizing the nateglinide.

56. A process for preparing nateglinide comprising the steps of:

a) converting trans-4-isopropylcyclohexanecarboxylic acid to trans-4-isopropylcyclohexane acid chloride by reaction with thionyl chloride in the presence of an organic amide;

b) adding the trans-4-isopropylcyclohexane acid chloride to an aqueous solution of sodium or potassium salt of D-phenylalanine in water free of a co-solvent; and

c) recovering the nateglinide.

57. A process for preparing nateglinide comprising the steps of:

a) converting 4-isopropylcyclohexanecarboxylic acid to 4-

isopropylcyclohexane acid chloride by reaction with thionyl chloride in the presence of an effective amount of an amide;

b) adding the isopropylcyclohexane acid chloride to a solution of sodium salt of D-phenylalanine in a mixture of acetone and water;

c) adding a water immiscible organic solvent to obtain an aqueous and an organic phase;

d) moving the nateglinide to the organic phase by reducing pH; and

e) concentrating the organic phase.